REMARKS

In the April 9, 2003 Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, the Examiner stated that this application contains sequence disclosures in Figure 1C that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §§ 1.821(a)(1) and (a)(2). The Examiner acknowledged that a computer readable form (CRF) of the sequence listing was previously submitted to the United States Patent and Trademark Office in connection with the subject application. The Examiner stated that, however, the disclosed sequence is not identified by a sequence identifier as required. The Examiner stated that applicants are required to amend the specification or amend the specification and CRF and the sequence listing, if the disclosed sequence is not present in the instant sequence listing.

The Notice states that applicants must provide a sequence identifier for Figure 1C. The Notice states that in the event that this sequence, i.e. the sequence in Figure 1C, is not a part of the instant sequence listing, applicants must provide: 1) an initial or substitute computer readable form (CRF) copy of the ''Sequence Listing''; 2) an initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification; and 3) a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §1.821(e) or §1.821(f) or §1.821(g) or §1.825(b) or §1.825(d).

In response, without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application, applicants have hereinabove amended the specification to include references to the sequence identifier information (i.e., SEQ ID NO:) as required by 37 C.F.R. §1.821(d). Pursuant to 37 C.F.R. §1.121(b)(1)(iii), applicants attach hereto as **Exhibit B** a

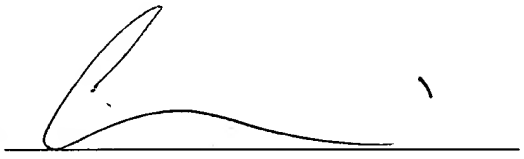
version of the amended paragraphs marked-up to show the changes relative to the previous version thereof. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested.

Applicants note that all sequences described in the subject application, including the sequence described in Figure 1C, were set forth in the ''Sequence Listing'' and accompanying CRF diskette which applicants previously submitted to the United States Patent Office on August 10, 2001. Therefore, applicants contend that they are not required to submit a substitute copy of the ''Sequence Listing,'' a computer readable form of the ''Sequence Listing'' or a statement pursuant to 37 CFR §1.821(f).

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, Mail Stop Sequence.

5/9/03
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EXHIBIT A

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/814,661	03/22/2001	Rodney Rothstein	56615-A-PCT-US/JPW/AJM/WW	2135

7590 04/09/2003

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EXAMINER	
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ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
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09/814,661

DEA/FCE-1994

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1mo: 5/9/03
2m: 6/9/03
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5m: 9/9/03
6m 10/9/03
W.D.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below a communication from the EXAMINER in charge of this application

Commissioner of Patents

1. This application contains sequence disclosures in figure 1C that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.R.F. § 1.821(a)(1) and (a)(2). A computer readable form (CRF) of the sequence listing was submitted. However, the disclosed sequence is not identified by a sequence idetifier as required. Applicant is required to amend the specification or amend the specification and the CRF and the sequence listing, if the disclosed sequence is not present in the instatn sequence listing.

2. Any questions regarding compliance with the sequence rules requirements specifically should be directed to Mark Spencer at 703-308-4212.

3. Applicant is given a TIME PERIOD of **ONE (1) MONTH** or **THIRTY (30) DAYS**, from the mailing date of this notice, whichever is longer, within which to supply the correction in order to avoid abandonment. EXTENSIONS OF THIS TIME LIMIT MAY BE GRANTED UNDER 37 CFR 1.136(a).

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Patent Examiner, Group 1642
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09/814,661

Application No. _____

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: Applicant must provide a sequence identifier for Fig. 1C. In the event that this sequence is not a part of the instant sequence listing, applicant must submit another CRF/Listing.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

EXHIBIT B

Marked-up Version of Amended Paragraphs

On page 5, lines 15-18, please delete the paragraph which begins "(Fig 1C) DNA sequence of the SML1 region. . ." and insert the following paragraph:

> (Fig 1C) DNA sequence of the SML1 region (SEQ ID NO: 1) is shown with the predicted amino acid sequence of the SML1 ORF (SEQ ID NO: 2). Two 11 base pair direct repeats are underlined. The putative TATA box is indicated by large bold letters.

On page 10, lines 29-35, please delete the paragraph which begins "The present invention provides . . ." and insert the following paragraph:

> The present invention provides for an isolated Sml1 protein or a homologue thereof. In one embodiment, the Sml1 protein has the amino acid sequence shown in Figure 1C ~~(Seq ID No. 1)~~. In another embodiment, the Sml1 protein is a homologue, such as a human Sml1 protein, a rat Sml1 protein, a mouse Sml1 protein, a microbial Sml1 protein, a plant Sml1 protein, or an insect Sml1 protein.

On page 44, lines 18-22, please delete the paragraph which begins "To follow the sml1-1 allele. . ." and insert the following paragraph:

> To follow the sml1-1 allele in genetic crosses, yeast colony PCR reactions were carried out (Adams et al., 1997). Using primer pair A (SEQ ID NO:3) and C (SEQ ID NO: 4) (Table 4), the wild-type and the sml1-1 alleles give rise to 570 bp and 280 bp PCR products, respectively.

On page 44, lines 24-37, please delete the paragraph which begins "To test whether overproduction. . ." and insert the following paragraph:

> To test whether overproduction of Mec1 rescues rad53 lethality, a GAL-MEC1 plasmid (pWJ701) was constructed. The native promoter of MEC1 on pRS416-MEC1 was replaced with a GAL1-10 promoter fragment (generated from a PCR reaction using primer pair p416-GAL 5' (SEQ ID NO: 9) and MEC1-GAL 3' (SEQ ID NO: 10), Table 4) through in vivo DNA recombination (Ma et al., 1987). This plasmid was then transformed into rad53Δ/RAD53 sml1-1/SML1 heterozygous diploids. After dissection of 66 total tetrads from six different transformants, no rad53Δ {pGAL-MEC1} spores were recovered on galactose-inducing medium. However, in the same dissections, the pRS416-MEC1 plasmid segregated into RAD53 or rad53 sml1 spores normally. Moreover, in a separate experiment, rad53Δ strains cannot lose a CEN-RAD53 plasmid (pWJ676) even when MEC1 is overexpressed.

On page 45, lines 8-19, please delete the paragraph which begins "Gene disruptions for . . ." and insert the following paragraph:

> Gene disruptions for SML1 and DUN1 were performed as described by Baudin et al. (1993). Forty-five base pairs of homology adjacent to each ORF was added to HIS3 and URA3 selectable markers, respectively, by PCR with the primers listed in Table 4 (SML1-HIS3 5' (SEQ ID NO: 5) & SML1-HIS3 3' (SEQ ID NO: 6) and dun1d 5' (SEQ ID NO: 7) & dun1d 3' (SEQ ID NO: 8)). MEC1 was disrupted in diploids using a fragment that contains the 800 bp TRP1 marker (from pUC18-TRP1) replacing the

sequence from 98 bp to 7764 bp (BamHI-SacII) of the MEC1 ORF (Rothstein, 1983). RAD53 was disrupted by transforming the EcoRI fragment containing rad53Δ::HIS3 (Zheng et al., 1993). All disruptions were confirmed by genomic blots and genetic analysis.

On page 47, lines 20-34, please delete the paragraph which begins "The strains and plasmids for . . ." and insert the following paragraph:

The strains and plasmids for two-hybrid analysis were PJ69-4A, pGBD-C2, pGAD-C2 (James et al., 1996) and pACTII (CLONTECH® Inc.). The primer pair pB-SML1 5' (SEQ ID NO: 11) and pGBD-SML1 3' (SEQ ID NO: 13) (Table 4) was used to amplify the SML1 ORF. After digestion with BamHI and PstI, this PCR product was cloned into the BamHI-PstI sites of pGBD-C2 to construct plasmid pWJ728. Similarly, plasmid pWJ684 contains a BamHI fragment from the PCR product of the SML1 ORF generated using the primer pair pB-SML1 5' and pB-SML1 3' (SEQ ID NO: 12) (Table 4) and inserted at the BamHI site of pACTII. PCR fragments containing the RNR1 or the RNR2 ORF were generated by primer pairs RNR1-ORF 5' (SEQ ID NO: 14) and RNR1 3' (SEQ ID NO: 15) or RNR2-ORF 5' (SEQ ID NO: 17) and RNR2 3' (SEQ ID NO: 16) (Table 4). These fragments were cloned into the BamHI-PstI site of pGBD-C2 and pGAD-C2 to construct pWJ731 and pWJ745 or pWJ729 and pWJ746 respectively.

On page 48, lines 6-16, please delete the paragraph which begins "The GST-Rnr1 fusion plasmid,. . ." and insert the following paragraph:

The GST-Rnr1 fusion plasmid, pWJ744, was generated by inserting a BamHI-SalI fragment from the PCR product of

the RNR1 ORF generated using primers RNR1-5'+0 (SEQ ID NO: 18) and RNR1 3' far (SEQ ID NO: 19) into the BamHI-SalI sites of pEG(KT) (Mitchell et al., 1993). The SML1 ORF was amplified using primer pYX-SML1 5' (SEQ ID NO: 20) and pB-SML1 3' and the BamHI-digested PCR product was cloned into BamHI site of pYX423. Next, an EcoRI fragment of a 3XHA tag (Schneider et al., 1995) generated after PCR using primer pair HA 5' (SEQ ID NO: 21) and HA 3' (SEQ ID NO: 22) was added to the N-terminus of SML1 to construct plasmid pWJ699. Both pWJ744 and pWJ699 can functionally complement rnr1 and sml1, respectively.

On page 51, lines 23-38, please delete the paragraph which begins "**Recombinant proteins and peptides.**" and insert the following paragraph:

Recombinant proteins and peptides. The recombinant yeast proteins Rnr1, Rnr2 and Rnr4 were expressed in E. coli BL21(DE3) bacteria using the pET3a expression vector; mouse recombinant proteins R1 and R2 were expressed in E. coli BL21(DE3)pLysS bacteria using the same vector (14). Purification of the recombinant mouse and yeast R1 proteins, and of the recombinant mouse R2 protein, was made as described earlier (15,16). The yeast Rnr2 and Rnr4 proteins were coexpressed and purified as a heterodimer[3]. The SML1 coding sequence (13) was amplified by PCR from yeast genomic DNA using the following oligonucleotides: 5'-CAA TAA TTT CCC CAT ATG CAA AAT TCC-3' (SEQ ID NO: 23) and 5'-AAA GGA TCC TTA GAA GTC CAT TTC CTC GAC-3' (SEQ ID NO: 24). After the PCR product was cleaved with NdeI and BamHI restriction endonucleases, it was cloned into the pET3a vector digested with the same restriction enzymes. The

SML1 sequence in the resulting plasmid was checked by DNA

On page 52, lines 15-17, please delete the paragraph which begins "N-acetylated peptides corresponding to . . ." and insert the following paragraph:

N-acetylated peptides corresponding to the last 9 amino acids of either Rnr2p (GAFTFNEDF) (SEQ ID NO: 25), Rnr4p (KEINFDDDF) (SEQ ID NO: 26) or Sml1p (QGKVEEMDF) (SEQ ID NO: 27) were ordered from Genosys.